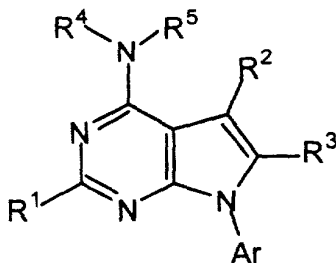


WHAT IS CLAIMED IS:

1. A compound of the formula:



or pharmaceutically acceptable salts thereof wherein

Ar is phenyl, 1- or 2-naphthyl, 2-, 3-, or 4-pyridyl, 2-, 4- or 5-pyrimidinyl, each of which is mono-, di-, or trisubstituted with halogen, trifluoromethyl, hydroxy, amino, cyano, carboxamide, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₃-C₇ cycloalkyl, or amino(C₁-C₆)alkyl with the proviso that at least one of the ortho or para positions of Ar is substituted;

R¹ is hydrogen, halogen, trifluoromethyl, carboxamide, carboxylate, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, or (C₁-C₆ alkyl)-G¹-R⁶ wherein G¹ is nitrogen, oxygen or sulfur and R⁶ is hydrogen, C₃-C₇ cycloalkyl, or C₁-C₆ alkyl;

R² and R³ together represent -(C₀-C₂)-G²-(C₂-C₄)- wherein G² is methylene, oxygen, sulfur or NR⁷, wherein R⁷ is hydrogen, C₃-C₇ cycloalkyl, or C₁-C₆ alkyl; or

R² and R³ taken together represent -CH=A-CH=CH- wherein

A is N or CR⁸;

R⁸ is -(C₀-C₆ alkyl)-Z;

Z is -CR⁹R^{9'}, NR⁹R^{9'}, OR⁹ or SR⁹; and

R⁹ and R^{9'} independently represent hydrogen or (C₁-C₆)alkyl;

R⁴ and R⁵ are the same or different and represent hydrogen, hydroxy, C₁-C₆ alkoxy(C₁-C₆)alkyl, hydroxy(C₁-C₆)alkyl, C₃-C₇ cycloalkyl, or C₁-C₆ alkyl; or

phenyl, 2-, 3-, or 4-pyridyl, 2- or 3-thienyl, or 2-,
4-, or 5-pyrimidinyl, each of which is
optionally mono- or disubstituted with halogen,
trifluoromethyl, hydroxy, C₁-C₆ alkyl, C₃-C₇
cycloalkyl, or C₁-C₆ alkoxy; or

R⁴ and R⁵ together represent -(C₂-C₃)-G³-(C₁-C₃)- where

G³ is methylene, 1,2 phenylene, oxygen, sulfur or
NR¹⁰; and

R¹⁰ is C₁-C₆ alkyl, C₃-C₇ cycloalkyl, phenyl, 2-, 3-,
or 4-pyridyl, 2- or 3-thienyl, or 2-, 4- or 5-
pyrimidyl.

2. A compound according to claim 1, wherein R₂ and R₃
together represent -CH=CR⁸-CH=CH-.

3. A compound according to claim 2, wherein R⁸ is
hydrogen or C₁-C₆ alkyl.

4. A compound according to claim 1, wherein Ar is phenyl
mono-, di-, or trisubstituted with halogen, trifluoromethyl,
hydroxy, amino, cyano, carboxamide, C₁-C₆ alkyl, C₁-C₆ alkoxy,
C₃-C₇ cycloalkyl, or amino(C₁-C₆)alkyl with the proviso that at
least one of the ortho positions of Ar is substituted.

5. A compound according to claim 4, wherein Ar is phenyl
substituted in the 2 and 4 positions with methyl, fluoro or
chloro.

6. A compound according to claim 3, wherein Ar is
2,4,6-trimethylphenyl.

7. A compound according to claim 6, wherein R⁴ and R⁵
independently represent hydrogen, C₁-C₆ alkoxy(C₁-C₆) alkyl, C₃-

C₇ cycloalkyl, or C₁-C₆ alkyl.

8. A compound according to claim 2, wherein R⁸ is -NR⁹R^{9'}.

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9. A compound according to claim 2, wherein R⁸ is -(C₁-C₆ alkyl)-NR⁹R^{9'}.

11. A compound according to claim 8, wherein Ar is 2,4,6-trimethylphenyl.

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10. A compound according to claim 8, wherein R⁴ and R⁵ independently represent hydrogen, C₁-C₆ alkoxy(C₁-C₆) alkyl, C₃-C₇ cycloalkyl, or C₁-C₆ alkyl.

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12. A compound according to claim 1, wherein R² and R³ together represent -(C₀-C₂)CH₂(C₂-C₄)-.

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13. A compound according to claim 12, wherein Ar is 2,4,6-trimethylphenyl.

14. A compound according to claim 13, wherein R⁴ and R⁵ independently represent hydrogen, C₁-C₆ alkoxy(C₁-C₆) alkyl, C₃-C₇ cycloalkyl, or C₁-C₆ alkyl.

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15. A compound according to Claim 1 which is 4-(N-Cyclopropylmethyl-N-propyl)amino-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

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16. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

17. A compound according to Claim 1 which is
4-(N-Propyl-N-methyl)amino-2-methyl-9-(2,4,6-trimethylphenyl)-
5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

5 18. A compound according to Claim 1 which is
4-(N-Cyclopropylmethyl-N-propyl)amino-2-methyl-9-(2,4,6-
trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

19. A compound according to Claim 1 which
10 4-(N,N-Dipropyl)amino-2-methyl-9-(2,4,6-trimethylphenyl)-9H-
pyrimidino[4,5-b]indole.

20. A compound according to Claim 1 which is
15 4-(N,N-Dipropyl)amino-6-ethylamino-2-methyl-9-(2,4,6-
trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

21. A compound according to Claim 1 which is
4-(N,N-Dipropyl)amino-6-diethylamino-2-methyl-9-(2,4,6-
trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

22. A compound according to Claim 1 which is
20 4-Bis(2-methoxyethyl)amino-2-methyl-9-(2,4,6-
trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-
b]indole.

23. A compound according to Claim 1 which is
25 4-(N,N-Dipropyl)amino-2-methyl-9-(4-bromo-2,6-
dimethylphenyl)-9H-pyrimidino[4,5-b]indole.

30 24. A compound according to Claim 1 which is
4-Bis(2-methoxyethyl)amino-2-methyl-9-(4-bromo-2,6-
dimethylphenyl)-9H-pyrimidino[4,5-b]indole.

25. A compound according to Claim 1 which is
4-(N,N-Dipropyl)amino-2-methyl-9-(4-chloro-2-methylphenyl)-
9H-pyrimidino[4,5-b]indole.

5 26. A compound according to Claim 1 which is
4-(N,N-Dipropyl)amino-2-methyl-9-(4-cyano-2,6-
dimethylphenyl)-9H-pyrimidino[4,5-b]indole.

10 27. A compound according to Claim 1 which is
4-Bis(2-methoxyethyl)amino-2-methyl-9-(2,4,6-
trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

15 28. A compound according to Claim 1 which is
4-(N-Cyclopropylmethyl-N-propyl)amino-6-ethylamino-2-methyl-
9-(2,4,6-trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

20 29. A compound according to Claim 1 which is
4-(N-(2-Hydroxyethyl)-N-Cyclopropylmethyl)amino-2-methyl-9-
(2,4,6-trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

30 30. A compound according to Claim 1 which is
4-(N-(2-Hydroxyethyl)-N-Cyclopropyl)amino-2-methyl-9-(2,4,6-
trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

25 31. A compound according to Claim 1 which is
4-(N,N-Dipropyl)amino-2-methyl-8-(2,4,6-trimethylphenyl)-
5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole

30 32. A compound according to Claim 1 which is
4-(N,N-Dipropyl)amino-2-methyl-9-(2,6-dimethylphenyl)-9H-
pyrimidino[4,5-b]indole.

33. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-2-methyl-9-(4-aminomethyl-2,6-dimethylphenyl)-9H-pyrimidino[4,5-b]indole.

5 34. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-2-methyl-9-(2,6-dimethyl-4-(methylaminomethyl)phenyl)-9H-pyrimidino[4,5-b]indole.

10 35. A compound according to Claim 1 which is 4-(N-Cyclopropylmethyl-N-propyl)amino-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

15 36. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

20 37. A compound according to Claim 1 which is 4-(N-Butyl-N-methyl)amino-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

25 38. A compound according to Claim 1 which is 4-(N-Propyl)amino-8-(2,4,6-trimethylphenyl)-5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole.

30 39. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-8-(2,4,6-trimethylphenyl)-5,6,7-trihydrocyclopenta[2,1-d]-8H-pyrimidino[4,5-b]indole.

40. A compound according to Claim 1 which is Ethyl 4-(dipropylamino)-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydropyrimidino[4,5-b]indole-2-carboxylate.

41. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-2-carboxyamido-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

5 42. A compound according to Claim 1 which is 4-(N,N-Dipropyl)amino-2-aminomethyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

10 43. A compound according to Claim 1 which is 4-(N-Cyclopropylmethylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

15 44. 4-(N,N-Dibutylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

20 45. 4-(N,N-Dibutylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

25 46. A compound according to Claim 1 which is 4-(N-(2-(4-Chlorophenyl)ethyl)amino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

47. A compound according to Claim 1 which is 4-(N-(2-(4-Chlorophenyl)ethyl)amino)-2-methyl-9-(2,4-dimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

30 48. A compound according to Claim 1 which is 4-(N-(4-Chlorophenyl)methylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

49. A compound according to Claim 1 which is 4-(N-(2-Methylphenyl)methylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

50. A compound according to Claim 1 which is 4-(N-(3-Trifluoromethylphenyl)methylamino)-2-methyl-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

51. A compound according to Claim 1 which is (N,N-Dipropylamino)-2-methyl-6-dimethylamino-9-(2,4,6-trimethylphenyl)-9H-pyrimidino[4,5-b]indole.

52. A compound according to Claim 1, which is 4-(N-Butyl-N-methyl)amino-9-(2,4,6-trimethylphenyl)-5,6,7,8-tetrahydro-9H-pyrimidino[4,5-b]indole.

53. A pharmaceutical composition comprising a compound according to claim 1 and at least one pharmaceutically acceptable carrier or excipient.

54. A process for preparing a compound according to Claim 1.

55. A packaged pharmaceutical composition comprising the pharmaceutical composition of Claim 53 in a container and instructions for using the composition to treat a patient in need thereof.

56. The packaged pharmaceutical composition of claim 55, wherein said patient is suffering from stress, posttraumatic

stress disorder, anxiety, depression, cardiovascular disease, headache, obesity or an eating disorder.

57. A method for localizing CRF receptors in tissue section
5 samples comprising:

contacting with a sample of tissue a detectably-labelled compound of Claim 1 under conditions that permit binding of the compound to the sample of tissue;

10 washing the tissue sample to remove unbound compound; and
detecting the bound compound.

58. A method for the treatment or prevention of physiological disorders associated with excess of or insufficient amount of CRF, which method comprises administration to a patient in need thereof an effect amount of a compound according to Claim 1.

59. A method of inhibiting the binding of CRF to the CRF1 receptor, which method comprises contacting, in the presence of CRF, a solution comprising a compound of Claim 1, with cells expressing the CRF1 receptor, wherein the compound is present in the solution at a concentration sufficient to reduce levels of CRF binding to IMR32 cells in vitro.

60. A method for altering the signal-transducing activity of a cell surface CRF1 receptor, said method comprising contacting cells expressing such a receptor with a solution comprising a compound according to Claim 1, wherein the compound is present in the solution at a concentration sufficient to reduce levels of
30 CRF binding to IMR32 cells in vitro.

61. A compound according to Claim 1 wherein in a standard assay of CRF binding the compound exhibits an IC_{50} of 1 micromolar or less.

5 62. A compound according to Claim 1 wherein in a standard assay of CRF binding the compound exhibits an IC_{50} of 100 nanomolar or less.

10 63. A compound according to Claim 1 wherein in a standard assay of CRF binding the compound exhibits an IC_{50} of 10 nanomolar or less.

15 64. A method for treating stress, posttraumatic stress disorder, anxiety or depression which comprises administering an effective amount of a compound according to Claim 1 to a patient in need thereof.

20 65. A method for treating obesity or eating disorders which comprises administering an effective amount of a compound according to Claim 1 to a patient in need thereof.

25 66. A method for treating cardiovascular disorders which comprises administering an effective amount of a compound according to Claim 1 to a patient in need thereof.

67. A method for treating headache which comprises administering an effective amount of a compound according to Claim 1 to a patient in need thereof.